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The role of astrocytes in memory: focus on pattern separation

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Western BrainsCAN
Transforming brain research.

Project **Summary**

KNOWLEDGE MOBILIZATION & IMPACT

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Background

Neurons are generally assumed to be the cells responsible for memory and cognition in our brain. We know they operate in networks, they exhibit electrical activity and can represent information through activity-based strengthening of connections between them. However, neurons only make up a small portion of the cells in the brain.

A much larger proportion is made of glial cells. Their role was traditionally assumed to be 'merely' supporting the neurons in a variety of ways, but this was perhaps only because they exhibited no electrical activity and because we had no tools to investigate them in living subjects.

Research in the last few years has been shining a light on these glial cells, particularly oligodendrocytes, microglia and especially astrocytes, and is finding that they may well have a much more significant role in memory and cognition than previously thought.

The Problem

One such example of this recent research is a study using mice models that were genetically engineered to replace much of their astrocytes with more complex human astrocytes. The mice exhibited faster learning and increased synaptic plasticity (the ability of synapses to strengthen and weaken in response to changes in activity, vital for memory and cognition).

We still need to be cautious in interpreting the research to date, as the existing tools used to manipulate astrocytes are not sufficiently selective to be certain that apparent changes in cognition were not because of 'off-target' effects (changes other than those intended, such as indirectly impacting neurons while intending to influence astrocytes).

The Project

New chemogenetic approaches are allowing us to target astrocytes directly to address this challenge, by combining these new approaches with the Cre/lox system of manipulating DNA at the level of specific cell types.

It has recently been shown that astrocytes play a leading role in a particular aspect of memory known as 'pattern separation' - differentiating between similar experiences or episodes in memory (say, recalling where you parked your car today compared to where you parked it yesterday). Pattern separation is disrupted in a wide variety of diseases of the brain so it is of considerable interest to memory researchers.

We have already shown in a small pilot study that we can improve pattern separation with selective manipulation of astrocytes in a specific brain region. In this project, we will attempt to demonstrate a clear relationship between astrocyte signalling and performance at pattern separation, and propose the underlying mechanisms of this influence of astrocytes on pattern separation.

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